VIII. DEVELOPMENT, LICENSURE, RECOMMENDATIONS FOR USE, AND POSTMARKETING SURVEILLANCE OF VACCINES

Ensuring the safety, efficacy, and consistency of vaccines is a critical part of the overall National Vaccine Program. A commitment that vaccines used in immunization programs be as free as possible from adverse consequences permeates all vaccine development and immunization efforts. Vaccine research, development, and licensure strive to ensure that the approaches selected and the candidates themselves are safe as well as effective. Appropriate use of vaccines is essential to maintain both the effectiveness and safety of immunization programs. Postmarketing surveillance (for example, phase IV studies) of vaccines also serves to monitor and assess safety.

The Food and Drug Administration (FDA) is responsible for the licensure of new vaccines and for ensuring that they continue to meet the prescribed standards for safety, purity, potency, and efficacy after approval. During development, candidate products are assessed in preclinical animal studies and clinical trials in humans (phases I, II, III) under investigational new drug applications. Upon completion of the clinical trials, a Product License Application (PLA) and an Establishment License Application (ELA) are prepared for the vaccine. The FDA reviews all phases of testing and, upon submission of the PLA and ELA, the agency reviews the adequacy of the data supporting safety and efficacy and issues a license if appropriate. The FDA is also responsible for establishing and monitoring compliance with standards for vaccines. The development of standards requires a scientific research basis; therefore the FDA conducts research to support this activity and also conducts research in other areas relevant to its mission. The FDA is also responsible for routine lot-by-lot release of all vaccines and for periodic inspections of vaccine manufacturing facilities.

Rapid and recent developments in biotechnology have identified new approaches to developing vaccines that may ultimately prove safer than those used historically. However, such developments require new approaches to vaccine assessment and licensure, and thereby place added stress on the current regulatory system.

With many new products in development, including combination vaccines, it is desirable to identify ways of simplifying the assessment of vaccines and of reducing the burden of prelicensure testing while maintaining safety standards. Expanding knowledge of correlates of immunity and of surrogate efficacy markers is critical to making available safe and effective vaccines. To this end, the FDA and other agencies undertake and support relevant research.

Appropriate use of vaccines is achieved in a variety of ways. The Vaccines and Related Biological Products Advisory Committee advises the FDA on issues relating to vaccine use as part of its mandate to provide advice on the FDA's regulatory decision making. Providers receive guidance on use through the use of approved labeling of products (package inserts). In addition, the Advisory Committee on Immunization Practices -- through the Centers for Disease Control and Prevention (CDC) -- makes recommendations on the use of vaccines, as do some specialty medical organizations, such as the American Academy of Pediatrics, which publishes its guidance in the so-called "Red Book," The public is given information on vaccination risks and benefits in the form of pamphlets on the vaccines that States require for school entry.

Postlicensure monitoring of possibly vaccine-related adverse events is also a priority. One system for postlicensure surveillance for safety is the Vaccine Adverse Event Reporting System (VAERS), which began operating on November 1, 1990. Jointly operated by the CDC and the FDA, VAERS provides a single national repository for the reporting of adverse events following the administration of all vaccines in the United States. VAERS can detect unusual clustering of serious adverse advents or clinical syndromes after vaccination.